

IN THE CLAIMS

1. (currently amended) A composition for generating an immune response in a mammal, said composition comprising:

(a) a polynucleotide component comprising a first polynucleotide consisting essentially of one polynucleotide ~~sequence which encodes encoding a first~~ an HIV immunogenic polypeptide derived from a first HIV strain, and

(b) a polypeptide component comprising ~~a second one or more~~ HIV immunogenic polypeptide ~~polypeptides~~ analogous to the first polypeptide ~~encoded by said polynucleotide component, with the proviso that at least one HIV immunogenic polypeptide of the polypeptide component is~~ and derived from a second HIV strain, wherein said first HIV strain and said second HIV strain are different.

2. (withdrawn—previously presented) The composition according to claim 1, wherein said second HIV strain is an HIV strain of the same subtype as said first HIV strain.

3. (previously presented) The composition according to claim 1, wherein said second HIV strain is an HIV strain of a different subtype than said first HIV strain.

4. (currently amended) A composition for generating an immune response in a mammal, said composition comprising:

(a) a polynucleotide component comprising:

a first two or more polynucleotide sequence sequences comprising a first coding sequence sequences for a first two or more analogous HIV immunogenic polypeptide; and polypeptides
a second polynucleotide sequence comprising a second coding sequence for a second HIV immunogenic polypeptide, wherein the first

and second HIV immunogenic polypeptides are derived from different HIV strains, and

(b) a polypeptide component comprising a third ~~one or more~~ HIV immunogenic polypeptide which is polypeptides analogous to the first and second polypeptides ~~polypeptide encoded by said polynucleotide component~~, with the proviso that, if the polypeptide component comprises two or more ~~the same number or greater than the number of analogous~~ HIV immunogenic polypeptides encoded by the polynucleotide component, then at least one of the two or more ~~HIV immunogenic polypeptides of the polypeptide component~~ is derived from a different HIV strain than the first and second HIV immunogenic polypeptides provided by the polynucleotide component.

5. (withdrawn—currently amended) The composition according to claim 4, wherein the first and second ~~said coding sequences for at least two of the~~ HIV immunogenic polypeptides are derived from different HIV strains of the same subtype.

6. (withdrawn—currently amended) The composition according to claim 5, wherein ~~said at least one HIV immunogenic polypeptides of the polypeptide component derived from a different HIV strain than the HIV immunogenic polypeptides provided by the polynucleotide component~~ the first, second, and third HIV immunogenic polypeptides are ~~is derived from a different HIV strains~~ strain of the same subtype as said HIV immunogenic polypeptides provided by the polynucleotide component.

7. (currently amended) The composition according to claim 4, wherein the first and second ~~said coding sequences for at least two of the HIV immunogenic polypeptides~~ are derived from different ~~HIV strains of different subtypes.~~

8. (currently amended) The composition according to claim 4, wherein ~~the third said at least one HIV immunogenic polypeptide polypeptides of the polypeptide composition derived from a different HIV strain than the HIV immunogenic polypeptides provided by the polynucleotide component~~ is derived from an a different HIV strain of a different subtype than the first and second ~~from said HIV immunogenic polypeptides provided by the polynucleotide component.~~

9. (withdrawn—previously presented) The composition according to claim 1, wherein ~~the first and second (i) the polynucleotide component does not encode an analogous HIV immunogenic polypeptides are polypeptide derived from HIV strains of the same any subtype other than the first subtype, and (ii) the polypeptide component does not comprise an analogous HIV immunogenic polypeptide derived from any subtype other than the first subtype.~~

10. (currently amended) A composition for generating an immune response in a mammal, said composition comprising:

(a) a polynucleotide component comprising:

a first two or more polynucleotide sequence sequences comprising a first coding sequence sequences for a first two or more analogous HIV immunogenic polypeptide polypeptides derived from a first different HIV strain; strains; and

a second polynucleotide sequence comprising a first coding sequence for a second HIV immunogenic polypeptide analogous to the first HIV immunogenic polypeptide and derived from a second HIV strain which is different from the first HIV strain; and

(b) a polypeptide component comprising a third one or more HIV immunogenic polypeptide polypeptides analogous to the first and second HIV immunogenic analogous

polypeptides ~~encoded by said polynucleotide component, wherein with the proviso that at least one of the~~ third HIV immunogenic ~~polypeptides of the polypeptide component~~ is derived from a different HIV strain than ~~the first HIV strain one of the analogous HIV immunogenic polypeptides provided by the polynucleotide component.~~

11. (currently amended) The composition of claim 10 wherein ~~the first and third one or more of the analogous~~ HIV immunogenic polypeptides are from different HIV subtypes.

12. (currently amended) The composition of claim 1, wherein said polynucleotide component ~~is a native polynucleotide or said the second HIV immunogenic polypeptide component comprises is a native polypeptide at least one polynucleotide that is a native polynucleotides or polypeptide.~~

13. (currently amended) The composition of claim 1, wherein said polynucleotide component ~~comprises at least one polynucleotide that~~ is a synthetic polynucleotide.

14. (original) The composition of claim 13, wherein said synthetic polynucleotide comprises codons optimized for expression in mammalian cells.

15. (original) The composition of claim 14, wherein said synthetic polynucleotide comprises codons optimized for expression in human cells.

16. (currently amended) The composition of claim 1, wherein the ~~polynucleotide component encoding an~~ first and second HIV immunogenic ~~polypeptides polypeptide and the polypeptide component comprising an HIV immunogenic polypeptide~~ are HIV envelope polypeptides.

17. (currently amended) The composition of claim 1, wherein ~~the at least one of said polynucleotide component, the first HIV immunogenic polypeptide, components encoding an~~

~~HIV immunogenic polypeptide and/or the second HIV immunogenic polypeptide at least one of said polypeptides~~ comprises an alteration or a mutation.

18. (currently amended) The composition of claim [[16]] 17 wherein ~~the first or second HIV immunogenic polypeptide is an HIV Env polypeptide and the said~~ alteration or mutation is selected from the group consisting of (1) a mutation in the cleavage site; (2) ~~a~~ a mutation in the glycosylation site; (3) a deletion of the V1 region; (4) a ~~a~~ modification of the V1 region; (5) a deletion in the V2 region; (6) a ~~a~~ modification of the V2 region; (7) a deletion of the V3 region; (8) a ~~a~~ modification of the V3 region; (9) a mutation that exposes a neutralizing epitope of ~~an~~ the HIV Env protein polypeptide; and (10) combinations thereof.

19 to 25. (canceled)

26. (currently amended) The composition of claim [[18]], 17 wherein at least one of ~~the first and second said HIV polypeptide immunogenic polypeptides~~ comprises an Env polypeptide ~~and wherein at least one of said envelope polypeptides is~~ modified to expose a CD4 binding region or an envelope binding region that binds to a CCR5 chemokine co-receptor.

27. (currently amended) The composition of claim 1, wherein ~~the first at least one polynucleotide encoding an HIV immunogenic polypeptide is encodes an immunogenic HIV polypeptide~~ selected from the group consisting of: Gag, Env, Pol, ~~Protease (Prot), Integrase (Int), Reverse Transcriptase (RT), Prot, Int, RT, vif, vpr, vpu, tat, rev, Vif, Vpr, Vpu, Tat, Rev, and Nef~~ nef.

28. (currently amended) The composition of claim 1, wherein the first HIV strain is an HIV subtype ~~is~~ selected from the group consisting of: subtype A, subtype B, subtype C, subtype D, subtype E, subtype F, subtype G, subtype H, subtype I, subtype J, subtype K, subtype N and subtype O.

29. (canceled)

30. (currently amended) The composition of claim 1, wherein said polynucleotide component further comprises a second polynucleotide sequence encoding one or more additional antigenic ~~polypeptide~~ polypeptides ~~which, with the proviso that the additional antigenic polypeptides are not an immunogenic polypeptides~~ derived from an HIV-1 strain.

31. (currently amended) The composition of claim 30, wherein said polypeptide component further comprises ~~a polypeptide having~~ an additional antigenic peptide, ~~with the proviso that the additional antigenic polypeptide which~~ is not ~~an immunogenic polypeptide~~ derived from an HIV-1 strain.

32. (currently amended) The composition of claim 1, wherein said polynucleotide component further comprises ~~sequences encoding one or more control elements~~ a control element compatible with expression in a selected host cell ~~and operably, wherein said control elements are operable~~ linked to the polynucleotide sequence ~~polynucleotides~~ encoding the first HIV immunogenic ~~polypeptide~~ polypeptides.

33. (currently amended) The composition of claim 32, wherein said control ~~element is~~ elements are selected from the group consisting of a transcription promoter, a transcription enhancer element, a transcription termination signal, a polyadenylation ~~sequence~~ sequences, a sequence ~~sequences~~ for optimization of initiation of translation, an internal ribosome entry site, and a translation termination ~~sequence~~ sequences.

34. (currently amended) The composition of claim 33, wherein said transcription promoter is selected from the group consisting of a CMV promoter, a CMV+intron A promoter, an SV40 promoter, an RSV promoter, an HIV-Ltr promoter, an MMLV-ltr promoter, and a metallothionein promoter.

35. (withdrawn—currently amended) A method of generating an immune response in a subject, comprising:

~~providing a composition for generating an immune response in a mammal according to claim 1;~~

~~administering one or more vectors comprising the polynucleotides of said polynucleotide component of the composition of claim 1 to the said subject under conditions that are compatible with expression of the first said polynucleotides in said subject for the production of encoded HIV immunogenic polypeptide polypeptides; and administering the polypeptide component to said subject.~~

36-37. (canceled)

38. (withdrawn—previously presented) The method of claim 35, wherein said polypeptide component further comprises an adjuvant.

39. (withdrawn—previously presented) The method of claim 35, wherein said polynucleotide component further comprises a carrier.

40. (withdrawn—currently amended) The method of claim 35, wherein the polynucleotide component comprises a ~~said one or more vectors are~~ nonviral vector ~~vectors~~.

41. (withdrawn—currently amended) The method of claim 35, wherein the polynucleotide component is ~~said one or more vectors are~~ delivered using a particulate carrier.

42. (canceled)

43. (withdrawn—currently amended) The method of claim 35, wherein the polynucleotide component is ~~said one or more vectors are~~ delivered using a PLG particle.

44. (withdrawn—currently amended) The method of claim 35, wherein the polynucleotide component is ~~said one or more vectors are~~ encapsulated in a liposome preparation.

45. (withdrawn—currently amended) The method of claim 44, wherein the polynucleotide component comprises a ~~said one or more vectors are~~ viral vector ~~vectors~~.

46. (withdrawn—currently amended) The method of claim 45, wherein the ~~said~~ viral vector is ~~vectors are~~ selected from the group consisting of a retrovirus vector, a lentivirus vector, an alphavirus vector, and an adenovirus vector ~~different subtypes, species or serotypes of viral~~ ~~vectors~~.

47-49. (canceled)

50. (withdrawn—currently amended) The method of claim ~~46~~ 45, wherein ~~said viral vectors are adenoviral vectors~~ the viral vector is an adenovirus vector.

51. (withdrawn—currently amended) The method of claim 50 wherein the adenovirus vector is a ~~said adenoviral vectors are~~ live replicating vector ~~vectors~~.

52. (withdrawn—currently amended) The method of claim 50 wherein the adenovirus vector is a ~~said adenoviral vectors are~~ non-replicating vector ~~vectors~~.

53. (withdrawn) The method of claim 35, wherein said subject is a mammal.

54. (withdrawn) The method of claim 53, wherein said mammal is a human.

55. (withdrawn) The method of claim 35, wherein said immune response comprises an adaptive immune response.

56. (withdrawn) The method of claim 55 wherein said immune response further comprises an innate immune response.

57. (withdrawn—currently amended) The method of claim 35, wherein the immune response is selected from the group consisting of ~~which comprises~~ an Antibody Dependent Cell Mediated Cytotoxic response, a humoral immune response, a cellular immune response, and combinations thereof.

58-59. (canceled)

60. (withdrawn—currently amended) The method of claim 35, wherein the polynucleotide component is ~~said one or more vectors are~~ administered intramuscularly, intramucosally, intranasally, subcutaneously, intradermally, transdermally, intravaginally, intrarectally, orally or intravenously.

61. (withdrawn—currently amended) The method of claim 35, wherein said immune response results in generating neutralizing antibodies in the subject against multiple strains derived from the one or more of said HIV ~~subtype~~ subtypes.

62. (canceled)

63. (withdrawn) The method of claim 35 wherein said immune response comprises the in vivo generation in said subject of broadly neutralizing antibodies that neutralize multiple HIV isolates.

64. (withdrawn) The method of claim 63 wherein said broadly neutralizing antibodies are characterized in that they demonstrate neutralizing activity to HIV strains utilizing the CCR5 coreceptor.

65. (withdrawn) The method of claim 63 wherein said broadly neutralizing antibodies are characterized in that they demonstrate neutralizing activity against two or more HIV strains from the same HIV subtype.

66. (withdrawn—currently amended) The method of claim 65 wherein said neutralizing antibodies demonstrate neutralizing activity against two or more HIV strains selected from the group consisting of ~~a the following HIV isolates~~ a Bal HIV isolate, a JR-FL HIV isolate, a Bx08 HIV isolate, a 6101 HIV isolate, a 692 HIV isolate, a 1168 HIV isolate, a 1196, and an ADA HIV isolate.

67. (withdrawn) The method of claim 63 wherein said broadly neutralizing antibodies are characterized in that they demonstrate neutralizing activity against two or more HIV strains from two or more different HIV subtypes.

68. (withdrawn—currently amended) The method of claim 67 wherein said neutralizing antibodies demonstrate neutralizing activity against two or more HIV subtypes selected from the group consisting of ~~the following~~ HIV subtypes: A, B, C, D, E, F, G, and O.

69. (withdrawn) The method of claim 35 wherein said immune response comprises the generation in said subject of antibodies that mediate Antibody Dependent Cell Mediated Cytotoxicity (ADCC).

70. (withdrawn) The method of claim 69 wherein said antibodies are characterized in that they demonstrate ADCC activity against two or more HIV strains from two or more different HIV subtypes.

71. (withdrawn—currently amended) The method of claim 70 wherein said antibodies demonstrate ADCC activity against two or more HIV subtypes selected from the group consisting of ~~the following~~ HIV subtypes: A, B, C, D, E, F, G, and O.

72. (withdrawn) The method of claim 69 wherein said broadly neutralizing antibodies are characterized in that they demonstrate neutralizing activity against two or more HIV strains from the same HIV subtype.

73. (withdrawn—currently amended) The method of claim 69 wherein said neutralizing antibodies demonstrate neutralizing activity against two or more HIV strains selected from the group consisting of ~~a the following HIV isolates:~~ Bal HIV isolate, ~~a~~ JR-FL HIV isolate, ~~a~~ Bx08 HIV isolate, ~~a~~ a 6101 HIV isolate, ~~a~~ a 692 HIV isolate, ~~a~~ a 1168 HIV isolate, ~~a~~ a 1196, and ~~an~~ ADA HIV isolate.

74-78. (canceled)

79. (currently amended) The composition according to claim 1, wherein said polypeptide component is ~~administered in the form of a protein~~ expressed on a virus like particle.

80. (currently amended) A composition for generating an immune response in a mammal, said composition comprising:

a polynucleotide component comprising a polynucleotide encoding a first ~~an~~ HIV immunogenic polypeptide derived from a first HIV strain, and

a polypeptide component comprising a second ~~an~~ HIV immunogenic polypeptide analogous to the first polypeptide and ~~encoded by said polynucleotide component, with the proviso that at least one HIV immunogenic polypeptide of the polypeptide component~~ ~~is~~ derived from a second HIV strain,

wherein said first HIV strain and said second HIV strain are different.

81. (withdrawn) A composition as in claim 80 wherein said second HIV strain is an HIV strain of the same subtype as said first HIV strain.

82. (original) A composition as in claim 81 wherein said second HIV strain is an HIV strain of a different subtype than said first HIV strain.

83. (canceled)

84. (currently amended) The composition of claim 4, wherein the first and second polynucleotide component encoding an HIV immunogenic polypeptides polypeptide and the polypeptide component comprising an HIV immunogenic polypeptide comprise HIV envelope polypeptides.

85. (currently amended) The composition of claim 4, wherein the at least one of said polynucleotide component, the first HIV immunogenic polypeptide, and/or the second components encoding an HIV immunogenic polypeptide and/or at least one of said polypeptides comprises an alteration or a mutation.

86. (currently amended) The composition of claim [[84]] 85, wherein said alteration or mutation is selected from the group consisting of (1) a mutation in the cleavage site; (2) a mutation in the glycosylation site; (3) a deletion of the V1 region; (4) a modification of the V1 region; (5) a deletion in the V2 region; (6) a modification of the V2 region; (7) a deletion of the V3 region; (8) a modification of the V3 region; (9) a mutation that exposes a neutralizing epitope of an the HIV Env protein polypeptide; and (10) combinations thereof.

87. (currently amended) The composition of claim [[86]] 85, wherein at least one of the first and second said HIV polypeptide immunogenic polypeptides comprises an Env polypeptide and wherein at least one of said envelope polypeptides is modified to expose a CD4 binding region or an envelope binding region that binds to a CCR5 chemokine co-receptor.

88. (currently amended) The composition of claim 4, wherein the first at least one polynucleotide encoding an HIV immunogenic polypeptide is encodes an immunogenic HIV polypeptide selected from the group consisting of: Gag, Env, Pol, Protease (Prot), Integrase (Int), Reverse Transcriptase (RT), Prot, Int, RT, vif, vpr, vpu, tat, rev, Vif, Vpr, Vpu, Tat, Rev, and Nef ~~nef~~.

89. (currently amended) The composition of claim 4, wherein the first HIV strain is an HIV subtype ~~is~~ selected from the group consisting of: subtype A, subtype B, subtype C, subtype D, subtype E, subtype F, subtype G, subtype H, subtype I, subtype J, subtype K, subtype N and subtype O.

90. (withdrawn—currently amended) A method of generating an immune response in a subject, comprising: ~~providing a composition for generating an immune response in a mammal according to claim 1;~~

administering ~~one or more vectors comprising the polynucleotides of said polynucleotide component of~~ the composition of claim 4 to ~~into~~ said subject under conditions that are compatible with expression of the first said polynucleotides in said subject ~~for the production of encoded HIV immunogenic polypeptide polypeptides; and~~ ~~administering the polypeptide component to said subject.~~